Abstract
Since early childhood obesity has increased dramatically in the recent year, many researchers observe the relationship of excess fat mass during childhood and many health consequences including with bone health. This review aims to examine the relationship between childhood obesity and bone health. The results are conflicting. Several results show that fat mass have a strong positive relationship with increase bone mass and bone area, while other studies found obesity may increase the risk of fracture and may be detrimental on bone health. By these findings, further studies should be conducted to examine the effect of childhood obesity and bone health, also to evaluate the mechanisms how excess fat mass may increase or reduce bone growth.

Introduction
Obesity has become an epidemic in many countries over the recent decade. World Health Organization notes that over one billion adults throughout the world are overweight, of whom around 300 million are obese. Also, several published studies suggested the increased prevalence of obesity among children and adolescent. Overweight and obese children have a larger body mass and require stronger and denser bones to carry their weight than their normal-weight peers. However, the effect of childhood obesity on bone health, particularly bone mineral accrual during growth periods is poorly understood.

Several recent studies report a positive relationship between total body fat mass and bone mass and bone area in young children. While other studies suggest that childhood obesity during growth does not increase bone mass and bone area to balance the excess weight. Furthermore, a study reported that higher body weight increased the risk of new fractures among young girls.

Regarding this concern, several possible mechanisms are described that body fat mass might result a negative effect on bone mass in young population. Adipose tissue has a high aromatase activity, and high amount of fat will contribute to increased serum steroid levels which might suppress periosteal bone growth. Moreover, the increased leptin concentration secondary to elevated fat mass has antiosteogenic function by decreasing bone mass via stimulation of sympathetic activity. Thus, hormones, growth factors, or inflammatory agents produced in adipose tissue may affect the suppression of bone growth.

On the other hand, higher fat mass might stimulate increases in bone size. Fat mass may promote skeletal growth through direct and indirect actions, a direct action on increasing lean body mass in obese children and indirect action on timing of pubertal events.

Obese children may have puberty earlier than their leaner counterparts due to higher estradiol and leptin levels. Puberty has a vital role in bone development since bone mass approximately doubles by the end of adolescence. The main factors of pubertal gain in bone mass are the sex steroids, growth hormones, insulin like growth factors.
and vitamin D. Therefore, it remains unclear whether obesity in childhood has positive or negative effects on bone mass and mineral accrual. This review aims to determine the effect of childhood obesity on bone health.

Studies which have noted a positive relationship between total fat mass and bone mass and/or bone area

Leonard et al (2004) have investigated the effect of childhood obesity on bone mass and dimensions in males and females relative to height, maturation and body composition. This study involved 132 non-obese subjects (body mass index (BMI) < 85th percentile) and 103 obese subjects (BMI ≥ 95th percentile). After 3-year follow up period, researchers found that the obese participants had greater lean body mass relative to height compared with non-obese subjects. Thus, obesity was significantly associated with larger whole–body bone area and bone mineral content (BMC) for age and for height after adjustment for maturation and lean mass.

One of the strengths of this cohort study, researchers used multivariate regression models to evaluate lean mass adjusted for sex, race, Tanner stage, and height between the obese and non-obese control subjects. Regarding these factors, findings suggest no sex interactions were observed and the adjusted models indicate that obesity, Tanner stage, Afro American race were independently and significantly related to greater lean body mass for height.

However, the authors have not described the rationale for the sample size in this study, whether this sample size was adequate enough to find the effect of childhood obesity on bone mass. Also, it seems that the authors did not consider some confounding factors that may influence skeletal mass and area such as nutritional diet and physical activity levels of the participants.

In 2003, Ellis et al carried out a study examining the relationship of bone mineral content and proportion of body fatness in 865 children. The study shows that obese children with the percentage of fat >30%, had higher BMC compared with children with normal adiposity (percentage of fat <25%) with matching criteria of age, gender, and ethnicity. However, when the result was adjusted for height, these differences were less significant. Authors suggest that obese children do not have lower whole-body BMC when compared with leaner children, even when adjusted for height, age, gender, and ethnicity.

A similar study was conducted by Goulding et al. (2008) investigating the relationship of childhood obesity and bone mass among 194 preschool New Zealand children. The finding showed a strong positive association between fat mass and total-body-less-head (TBLH) area and TBLH bone mineral content (BMC) in both sexes after adjustment for socioeconomic status (SES), ethnic group, lean mass and height. This result is consistent with British birth cohort study conducted in older children.

From the findings, regarding increased weight, the range of fat mass is greater than the range of lean mass. The results demonstrated that TBLH bone area raised by 12.8 cm² in boys and 9.4 cm² in girls for every kilograms increase in fat mass independently of height and lean mass. Some limitations of the study included no
detailed information about the amount of energy intake and energy expenditure, and no report of weight-bearing physical activity, hormone levels, bone and muscle strength. However, there are several strengths of this study, such as the recruitment from a birth cohort study, specific age range of the samples, comprehensive assessments of body composition, and bone measurement without head area. All these factors support researcher to focus in analysing the skeleton most responsive in affecting bone size.

Clark et al. (2006) carried out a study examining the relationship between obesity and bone mass area in children aged 9.9 years and the increase of bone mass and area over the following 2 years. The result indicated a strong positive association between total body fat mass and TBLH bone mass and area after adjustment for height and/or lean mass.

The same authors also found a similar positive relationship between total body fat mass and the increase of bone mass and area over the subsequent 2 years in boys and Tanner stage 1 girls. Conversely, there were no association and a negative association between total fat mass and bone mass and size in Tanner stage 2 and stage 3 girls respectively.

Based on these findings, this study provides strong evidence that adipose tissue promotes bone development in pre-pubertal children. However, the relationship is diminished by puberty. Since only minimal effect was observed by additional adjustment for height, these findings suggest that fat mass acts to stimulate bone size on radial rather than longitudinal bone growth.

The authors suggested some possible mechanisms for their findings. Some evidence indicates a positive relationship between leptin and changes of bone area in pre-pubertal girls. Moreover, fat mass in pre-pubertal period is related to serum IGF-1 and esterogen which are known to influence bone growth.

Studies which have noted a negative relationship between total fat mass and bone mass and/or bone area

In 2000, Goulding et al. conducted a study to determine the relationship between total bone mass or total bone area to total body weight in obese and overweight children compared with normal-weight children. Researchers involved fracture-free children in this study. They found that overweight and obese children had smaller bone mass and bone area for their body weight compared with normal weight children during growth spurt.

They assume that the gap between higher body weight and bone development during growth may result in significant burden for the bones and joints of children with excess body weight. This condition may cause lasting joint damage resulting osteoarthritis in adulthood. Thus, obesity in young children is a determined risk factor for adult osteoarthritis. In line with this finding, the earlier study by McCormick et al. (1991) also reported a reduced spinal density in increased body weight in obese participants.

Evidence of adaptive increases in BMC relative to both lean mass and fat mass was observed in obese children indicating skeletal compensation to increase bone mass.
However, the obtained BMC values significantly lower than predicted BMC values relative to weight in overweight groups.

There are several limitations of this study. Since the subjects of this study were volunteers, thus may not be a representative sample of existing New Zealand young population. Furthermore, investigators did not assess physical activity levels and hormone concentration of participants that definitely influence skeletal growth and mineral accrual.

In contrast, this study has several strengths. This cross-sectional survey involved a wide range of participants of both genders and age, assessed precise measurements of body composition using DXA and used well-accepted BMI classification of overweight and obesity. Researchers analysed the predictions by using regression measurement that provided moderate estimations of expected bone mineral content of particular adiposity groups.

In the same year, Goulding et al (2000) examined some predictors of childhood fractures. They conducted a cohort study involving both young girls who had broken a forearm and fracture free. The results showed that participants with previous fractures and low total areal bone mineral density (aBMD), or previous fractures and high body weight, or previous fractures and low spinal bone mineral apparent density (BMAD) have significantly higher fracture risks compared to girls with single risk factor. In accordance with the findings, researchers suggest that increasing bone mineral density and decreasing body weight will have the possibility to reduce fractures.

However, there are some limitations of this study. Researchers did not gather the information related to family history, frequency of falling, or changing patterns in nutrition and physical activity of participants. Thus, researchers cannot show whether risk-taking behaviour differs in girls had new fractures. They also realised that sample size may not have been big enough to determine the ability of aBMD values as the predictor of new fractures with a wide intra- and inter-subject variations in growing period. Conversely, using a high proportion of girls having a history of fracture brings a benefit of this study to identify the significant predictors of new fractures in young population.

Goulding et al (2002) carried out a study evaluating whether overweight and obese children in both sexes have adequate compensatory increases in bone mineral content (BMC) particularly in vertebral and lumbar spine area to adjust their excess body weight. The results indicated that overweight and obese children in both sexes do not increase their spinal BMC to completely compensate their excessive weight.

During growth periods, heavy loading on the spine is harmful. Although the spine of the growing skeleton may be more adaptable than those of adults, increased mechanical load on backs of obese children could contribute injury in the intervertebral joints as well as within the bone. Thus, low back pain is related to obesity. A study reported that low back pain and spinal damage commonly occur at growth period, particularly when there are disconnections between body weight and bone mineral content.

Moreover, based on a meta-analysis evaluated the relationship between
overweight/obesity and low back pain, obesity was associated with the increased prevalence of low back pain. They found that overweight subjects had a higher prevalence of low back pain than normal-weight people but a lower prevalence compared with obese subjects. These findings suggest that overweight and obesity increase the risk of low back pain.\textsuperscript{21}

**Discussion and possible reasons for differing study findings**

There are several possible reasons that may influence study findings. The reviewed studies have different research methodologies including the setting of the studies, study design, sample size, the length of the study and study population. All these differences may affect outcomes.

In terms of study design, one study was carried out in combined cross-sectional and prospective cohort studies, one in case control study and two in cross sectional studies. Three in cohort studies. Thus, regarding the hierarchy of evidence, cohort studies are stronger than case-control and cross sectional studies.\textsuperscript{2,4,6,7,8,12,16}

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<td>Goulding et al, 2000</td>
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*: Studies show positive relation between childhood obesity and bone health

From table 1 we can see that most studies in cohort found a positive association between increase fat mass during childhood and bone health, while all the cross sectional studies showed a negative relationship. It seems that studies indicated fat mass have a strong positive relationship on bone mass have stronger research design.
The studies also have different setting for study, some in a clinical setting and some in population 2,5,6,12.

It seems that most of the reviewed studies have different study duration. Greenhalgh (1997) notes that a cohort study should provide a sufficient follow up period to see the outcomes of the exposures. The effects of obesity in bone mass may not be seen in the studies which have insufficient time duration 9.

Although all of reviewed studies are carried out among children, they were conducted in the different study population which may have some different factors such as age, ethnicity, and socioeconomic status which may also influence body weight and bone development. Moreover, most of the studies have different sample sizes. An adequate sample size is important in finding a statistically significant effect in a study (IFIC, 2001). In one study, researcher notes that one of the limitations of their study is that sample size may not be big enough to determine the ability of aBMD values to predict new fractures with a wide intra- and inter-subject variation in growing period 5.

The different outcomes related to bone strength, Clark et al. (2006) found that fat mass may act to stimulate radial bone growth resulting in a larger long-bone cross sectional area which is predicted to increase bone strength. In contrast, a previous study showed that obesity is related to an increased risk of fracture among young population. The possible reasons of this difference is although fat mass commonly acts to improve periotosteal skeletal growth, there is a subset of children with flawed responses in whom the risk of fracture increases. Thus, bone size relative to obesity, rather than each factor alone, may be an important determinant of fracture risk in young population 5,12.

Moreover, most of these reviewed studies did not assess some confounding factors such as nutritional intake and physical activity levels of participants that undoubtedly influence bone growth and mineral accrual. Physical activity is an important cofactor to achieve maximal peak bone mass during growth period. In any study design, those factors should be identified and included in the assessment. Margetts et al. (2002) notes that observational studies, particularly case-control studies are more subject to bias. Thus, researchers should minimize or avoid biases by measuring the effect of these biases on the outcomes before the study can be properly interpreted 15,16,24.

**Conclusion**

Based on this review, studies of the effect of childhood obesity on bone mass and mineral accrual during growth period yielded inconsistent outcomes. Some studies have found a positive relationship between total fat mass and bone mass and/or bone area while others suggest that fat mass may decrease bone growth and increase the risk of fracture in children 4,5,6,7,12.

The different findings might be due to several possible factor such as different research methodologies including the setting of the studies, study design, sample size, study duration and study population. All these differences may affect different outcomes. In term of study design, one study was carried out in combined cross-sectional and prospective cohort studies, one study
used case control design, two in cross sectional, and three in cohort studies.

Thus, regarding the hierarchy of evidence, cohort studies are stronger than case-control and cross sectional studies. Most studies with higher hierarchial study design have showed a strong positive association between childhood obesity and bone health. Further research is required to determine the mechanisms by which excess fat mass may increase or reduce bone growth.

References

10. International Food Information Council Foundation, IFIC. How to understand and interpret food and health-related scientific studies. IFIC review. 2001; 9(1), 1-11.


